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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/755,251	01/05/2001	Sergio Abrignani	CHIR-0309	6900

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EXAMINER
WORTMAN, DONNA C

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 06/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/755,251	ABRIGNANI, SERGIO	
	Examiner	Art Unit	
	Donna C. Wortman, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 Jan 2003; 21 Apr 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-23 and 25-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-23 and 25-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *09/011,910* .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Claims 21-23 and 25-29 were amended and claims 24 and 30-40 were canceled in Paper No. 18 filed January 16, 2003.

Claim 21 is drawn to a method of treating a patient infected with HCV comprising administering to the patient an unglycosylated, transmembrane protein having a molecular weight of about 24 kd, or a fragment of the protein, wherein the protein or the fragment specifically binds to the E2 protein of HCV. Claims 22 and 25-29 are drawn to a composition comprising the same protein or fragment as that recited in claim 21 in combination with a pharmaceutically acceptable carrier. Claims 26-29 recite the protein component of the composition in product-by -process form. Claim 23 is drawn to a method for preparing a composition comprising combining the protein or fragment with a pharmaceutically acceptable carrier.

Rejections moot/withdrawn

The rejection of claims 24 and 30-40 under 35 USC 112, second paragraph, is made moot by the cancellation of those claims, and is withdrawn for claims 21-23 and 25-29 in view of Applicant's amendments to the claims and the remarks on page 13 of Paper No. 18.

The rejection of claims 24 and 30-40 under 35 USC 112, first paragraph, as lacking written description and not being enabled is made moot by the cancellation of those claims, and is withdrawn for claims 21-23 and 25-29 in view of the amendments to the claims, which no longer recite "variants" and which recite only specifically binding protein fragments, and in view of Applicant's remarks in paragraph (C) on pages 11-12 of Paper No. 18.

The rejections of claims 21-40 under 35 USC 112, second paragraph, are withdrawn in view of Applicant's cancellation of claims 24 and 30-40 and amendments to claims 21-23 and 25-29. The rejection of claim 27 under 35 USC 112, second paragraph, for reciting "hyperexpresses" is withdrawn in view of Applicant's remarks at page 13, last paragraph, pointing out that the specification teaches that hyperexpression requires that the expression of the 24 kD protein be greater than the original. Hyperexpression of the 24 kD protein is understood to be any amount of expression by a mammalian cell that is greater than that in the original mammalian cell.

Rejections maintained, and applied to amended claims

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21-23 and 25-29 as last amended are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, essentially for reasons of record in rejecting claims 21-23 in the previous Office action, Paper No. 15, at pages 2-4.

Applicant has argued that sufficient information has been provided to enable one of skill in the art to make and use the invention as claimed; that HCV E2 has been shown to bind to the purified 24 kD protein and cells expressing the 24 kD protein; that later reports confirm that CD81 binds to an HCV E1E2 that is properly folded and

interacts with conformation-dependent monoclonal antibodies and cites Lambot et al., cited on PTO 1449; that the information in the specification asserting that "making available a soluble form of the protein of the invention will act as an antagonist of binding of HCV to the cellular receptor thus reducing or preventing the infection process and thereby treating the disease" should be accepted; and cites Pileri et al. and Petracca et al. and asserts that it is of no consequence that additional factors might be needed for infectivity or internalization, since binding alone leaves less circulating virus and therefore serves to decrease viral load, which is generally desirable. Applicant has argued that only claim 21 relates to a method of treatment, while claims 22 and 23 (actually claims 22, 23, and 25-29) are drawn to a composition and method of making a composition, and that limitations have been imported from the specification into the claims, since one possible use of the composition is not an element of the rejected claims. Applicant has pointed to other disclosed uses for the proteins and compositions.

Applicant's arguments have been considered but not found persuasive. Since claims 22-29 recite "a pharmaceutically acceptable carrier," they are interpreted, for the purposes of analysis of enablement, to be drawn to pharmaceutical compositions and a method of making a pharmaceutical composition. "Pharmaceutically acceptable carrier" is clearly recited and is not "imported from the specification." For the claims to be enabled, the specification must teach how to use the composition for at least one pharmaceutical use without undue experimentation. The only pharmaceutical use disclosed is as a treatment for a patient infected with HCV. The references cited by

Applicant provide additional evidence that CD81 specifically binds E2 of HCV; binding capability has not been disputed here. It is not at all apparent that the binding of a CD81 protein to HCV *in vitro* could be extrapolated to the same capacity to bind HCV *in vivo*, since, for example, HCV in an infected individual is likely to be complexed with antibodies and/or lipoproteins, and it is not known to what extent the existence of these complexes would be likely to affect the binding of CD81 to HCV. Further, HCV E2 comprises a hypervariable region, and it is not apparent that all variant HCV E2's would be expected to retain the capability to bind a CD81 protein. Applicant has asserted that "binding alone leaves less circulating virus and therefore serves to decrease viral load" but has provided no factual evidence that Applicant's 24 kD protein, otherwise known as CD81, if bound to HCV *in vivo*, would actually result in a decreased viral load.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 22 and 24-29 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Levy et al. 1991 (The Journal of Biological Chemistry 266(22):14597-14602, 1991), taken in light of Levy et al. 1998 and

Pileri et al. (Science 282:938-941, 1998), for reasons of record. With respect to claims 26-29, where the protein portion of the composition is recited in product-by-process format, in the absence of factual evidence to the contrary, the 24 kD protein as recited is the same as the protein of Levy 1991, regardless of the method by which it was obtained or prepared. As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith. In re Brown, 459 F.2d 531, 535,173 USPQ 685, 688 (CCPA 1972).

First, Applicant correctly assumes that the rejection is made over Levy et al., 1991; Levy et al. 1998 and Pileri et al. 1998 were cited as evidence of the identification of TAPA-1 and CD81 as the same protein and of the inherent properties of TAPA-1. Applicant has argued that Levy et al. 1991 does not describe a composition or method of use as claimed and quotes Levy as stating that the functions of the TAPA-1 related family of proteins are currently unknown.

These arguments have been considered but not found persuasive. First, claim 21, drawn to a method of treatment, is not rejected over Levy et al. The other claims, drawn to compositions and methods of making compositions, are not distinguished over any of the TAPA-1 preparations disclosed by Levy et al., since Applicant's broadly recited "pharmaceutically acceptable carrier" is not distinguished from Levy et al.'s various solutions and buffers in which TAPA-1 appears (phosphate buffered saline or resuspension buffer, e.g.).

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 22 and 24-29 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 17 of copending Application No. 09/011910. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claims 22 and 24-29 are drawn to the same protein and compositions comprising that protein as is claim 17 of Application No. 09/011910, which is drawn to a (kit) composition that does not recite any components except the protein; the instant claims are not distinguished from claim 17 of Application No. 09/011910 since the protein and the composition are the same regardless of their intended use.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 22 and 24-29 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 7 and 27-31 of copending Application No. 09/509612. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are

drawn to treatment methods, a pharmaceutical composition and a method of making the pharmaceutical composition that use the same protein as the treatment methods recited in claims 7 and 27-31 of Application No. 09/509612 and thus would have been obvious over the treatment methods of claims 7 and 27-31.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant has indicated, in Paper No. 20 filed April 21, 2003, at least for Application No. 09/509612, that since prosecution continues in both cases, Applicant will consider filing a terminal disclaimer once allowable subject matter is indicated.

The provisional obviousness type double patenting rejections over claim 17 of 09/011910 and over claims 7 and 27-31 of 09/509612 are maintained since there is no reason to withdraw them at this time.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna C. Wortman, Ph.D. whose telephone number is 703-308-1032. The examiner can normally be reached on Monday-Thursday, 7:30-5:00 and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Donna C. Wortman, Ph.D.
Primary Examiner
Art Unit 1648

dcw
June 26, 2003